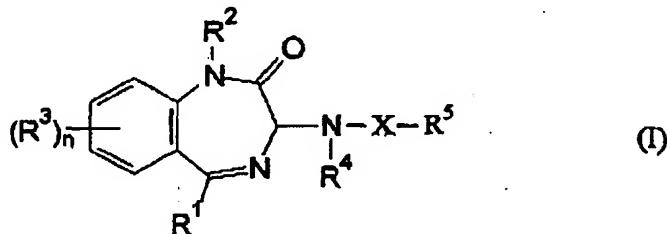


CLAIMS

1. Use of a compound which is (a) a benzodiazepine derivative of the formula (I) or an N-oxide thereof or (b) a pharmaceutically acceptable salt thereof, in the
 5 manufacture of a medicament for use in treating or preventing an RSV infection



wherein:

- R^1 represents C_{1-6} alkyl, aryl or heteroaryl;
- 10 - R^2 represents hydrogen or C_{1-6} alkyl;
- each R^3 is the same or different and represents halogen, hydroxy, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, amino, mono(C_{1-6} alkyl)amino, di(C_{1-6} alkyl)amino, nitro, cyano, $-CO_2R'$, $-CONR'R''$, $-NH-CO-R'$, $-S(O)R'$, $-S(O)_2R'$, $-NH-S(O)_2R'$, $-S(O)NR'R''$ or $-S(O)_2NR'R''$, wherein each R' and
- 15 R'' is the same or different and represents hydrogen or C_{1-6} alkyl;
- n is from 0 to 3;
- R^4 represents hydrogen or C_{1-6} alkyl;
- X represents $-CO-$, $-CO-NR'$, $-S(O)-$ or $-S(O)_2-$, wherein R' is hydrogen or a C_{1-C_6} alkyl group; and
- 20 - R^5 represents an aryl, heteroaryl or heterocyclyl group, which group is substituted by a C_{1-C_6} hydroxyalkyl group or a $-(C_{1-C_4} \text{ alkyl})-X_1-(C_{1-C_4} \text{ alkyl})-X_2-(C_{1-C_4} \text{ alkyl})$ group, wherein X_1 represents $-O-$, $-S-$ or $-NR'$, wherein R' represents H or a C_{1-C_4} alkyl group and X_2 represents $-CO-$, $-SO-$ or $-SO_2-$, or R_5 represents $-A_1-Y-A_2$, wherein:
- 25 - A_1 is an aryl, heteroaryl, carbocyclyl or heterocyclyl group;
- Y represents a direct bond or a C_{1-C_4} alkylene, $-SO_2-$, $-CO-$, $-O-$, $-S-$ or $-NR'$ moiety, wherein R' is a C_{1-C_6} alkyl group; and

- A₂ is an aryl, heteroaryl, carbocyclyl or heterocyclyl group.

2. Use according to claim 1, wherein R¹ is C₁₋₂ alkyl or phenyl.

5 3. Use according to claim 1 or 2, wherein R² is hydrogen.

4. Use according to any one of the preceding claims wherein R³ is halogen, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylthio, C₁₋₄ haloalkyl, C₁₋₄ haloalkoxy, amino, mono(C₁₋₄ alkyl)amino or di(C₁₋₄ alkyl)amino.

10 5. Use according to claim 4, wherein R³ is fluorine, chlorine, bromine, C₁₋₂ alkyl, C₁₋₂ alkoxy, C₁₋₂ alkylthio, C₁₋₂ haloalkyl, C₁₋₂ haloalkoxy, amino, mono(C₁₋₂ alkyl)amino or di (C₁₋₂ alkyl)amino.

15 6. Use according to any one of the preceding claims wherein R⁴ is hydrogen or C₁₋₂ alkyl.

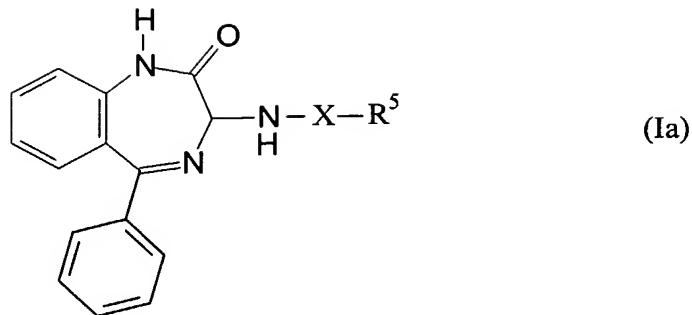
7. Use according to any one of the preceding claims wherein X is -CO- or -CO-NR'- wherein R' represents hydrogen or a C₁-C₂ alkyl group.

20 8. Use according to any one of the preceding claims, wherein R⁵ is a 5- or 6-membered heterocyclyl or heteroaryl ring which is substituted by a C₁-C₆ hydroxyalkyl group or a -(C₁-C₄ alkyl)-X₁-(C₁-C₄ alkyl)-X₂-(C₁-C₄ alkyl) group, wherein X₁ and X₂ are as defined in claim 1.

25 9. Use according to claim 8, wherein R⁵ is a 5- or 6- membered heteroaryl group which is substituted by a -CH₂-OH or -(C₁-C₄ alkyl)-NR'-(C₁-C₄ alkyl)-S(O)₂-(C₁-C₄ alkyl) substituent, wherein R' is hydrogen or C₁-C₂ alkyl.

30 10. Use according to any one of the preceding claims, wherein A₁ is an aryl or heteroaryl group.

11. Use according to claim 10, wherein A₁ is a phenyl group, a monocyclic 5- or 6- membered heteroaryl group or a 5- to 6- membered heteroaryl group fused to a monocyclic oxo-substituted 5- to 6- membered heterocycl group.
- 5 12. Use according to any one of the preceding claims wherein A₁ is unsubstituted or substituted by 1 or 2 substituents selected from halogen, cyano, nitro, C₁-C₄ alkyl, C₁-C₄ haloalkyl and C₁-C₄ alkoxy substituents.
- 10 13. Use according to any one of the preceding claims, wherein Y represents a direct bond, a C₁-C₂ alkylene group, -SO₂- or -O-.
14. Use according to any one of the preceding claims, wherein A₂ is a phenyl, 5- to 6- membered heteroaryl, 5- to 6- membered heterocycl or C₃-C₆ cycloalkyl group.
- 15 15. Use according to any one of the preceding claims, wherein when A₂ is a heterocycl group it is attached to the moiety Y via a N atom.
- 20 16. Use according to any one of the preceding claims, wherein A₂ is unsubstituted or is substituted by 1 or 2 substituents which are selected from C₁-C₄ alkyl and halogen substituents when A₂ is a heteroaryl or aryl group and which are selected from C₁-C₄ alkyl, halogen and oxo substituents when A₂ is a carbocyclic or heterocycl group.
- 25 17. Use according to any one of the preceding claims, wherein A₂ is a piperazinyl, pyridyl, morpholinyl, pyrrolidinyl, piperidinyl, pyrazinyl, cyclopropyl, phenyl or S,S-dioxo-thiomorpholino group, which is unsubstituted or substituted by a C₁-C₂ alkyl group.
- 30 18. Use according to any one of the preceding claims wherein the benzodiazepine derivative of formula (I) is a benzodiazepine derivative of formula (Ia):



wherein:

- X is -CO- or -CO-NH- ; and
- 5 - R⁵ is a 5- to 6- membered heteroaryl group, for example a furanyl group, which is substituted by -CH₂-OH or -(C₁-C₄ alkyl)-N(CH₃)-(C₁-C₄ alkyl)-SO₂-(C₁-C₄ alkyl) or R₅ represents -A₁-Y-A₂, wherein:
 - A₁ is a phenyl, pyridyl, furanyl, thiazolyl, oxazolyl, isoxazolyl, thienyl or 1H-imidazo[4,5-b]pyridin-2-(3H)-one moiety, which is unsubstituted or substituted by 1 or 2 substituents selected from halogen, cyano, C₁-C₂ alkyl, C₁-C₂ haloalkyl and C₁-C₂ alkoxy substituents;
 - Y is a direct bond, a C₁-C₂ alkylene group, -SO₂- or -O-; and
 - A₂ is a piperazinyl, pyridyl, morpholinyl, pyrrolidinyl, piperidinyl, pyrazinyl, cyclopropyl, phenyl or S,S-dioxo-thiomorpholino group, which is unsubstituted or substituted by a C₁-C₂ alkyl group.

19. Use according to any one of the preceding claims, wherein the medicament is for use in treating a patient who is a child under two years of age, an adult suffering from asthma, chronic obstructive pulmonary disorder (COPD) or immunodeficiency, 20 an elderly person or a person in a long term care facility.

20. Use according to claim 19 wherein said child suffers from chronic lung disease.

25 21. Use according to any one of claims 1 to 18 wherein the medicament is for use in preventing RSV infection in an infant less than six years of age who was born after 32 weeks of gestation or less.

22. Use according to any one of the preceding claims, wherein the medicament is suitable for intranasal or intrabronchial administration.

5 23. Use according to any one of the preceding claims, wherein the medicament further comprises an anti-inflammatory compound or an anti-influenza compound.

24. Use according to claim 23 wherein the anti-inflammatory compound is budesonide or fluticasone.

10

25. Use according to claim 23 wherein the anti-inflammatory compound is a leukotriene antagonist, phosphodiesterase 4 inhibitor or TNF alpha inhibitor.

15

26. Use according to claim 23 wherein the anti-inflammatory compound is an interleukin 8 or interleukin 9 inhibitor.

27. Use according to any one of claims 1 to 22 wherein the medicament is coadministered with an anti-inflammatory compound, as defined in any one of claims 24 to 26, or an anti-influenza compound.

20

28. A method of treating a patient suffering from or susceptible to an RSV infection, which method comprises administering to said patient an effective amount of a compound as defined in any one of claims 1 to 18.

25

29. A method according to claim 28, wherein said patient is a patient as defined in any one of claims 19 to 21.

30. A method according to claim 28 or 329, wherein said compound is administered intranasally or intrabronchially.

30

31. An inhaler or nebuliser containing a medicament which comprises
(a) a compound as defined in any one of claims 1 to 18, and

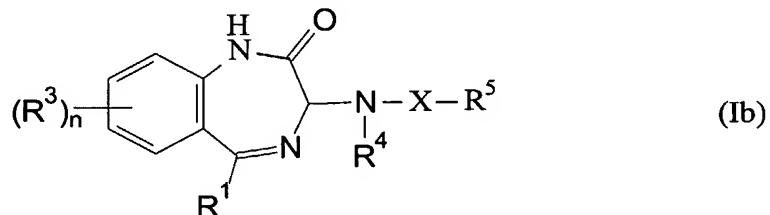
(b) a pharmaceutically acceptable carrier or diluent.

32. A product comprising a compound as defined in any one of claims 1 to 18 and an anti-inflammatory compound, as defined in any one of claims 24 to 26, or an anti-influenza compound.

33. Use of a product according to claim 32 in the manufacture of a medicament for use in the treatment of concomitant RSV and influenza infections.

10 34. Use of a compound as defined in any one of claims 1 to 18 in the manufacture of a medicament for use in the treatment of human metapneumovirus, measles, parainfluenza viruses, mumps, yellow fever virus (B5 strain), Dengue 2 virus or West Nile virus.

15 35. A compound which is (a) a benzodiazepine derivative of formula (Ib) or an N-oxide thereof, or (b) a pharmaceutically acceptable salt thereof



20 wherein R_1 , R_3 , n , R_4 , X and R_5 are as defined in any one of claims 1 to 18.

36. A compound according to claim 35, wherein R₁ is an unsubstituted phenyl group.

25 37. A compound according to claim 35 or 36, wherein when A_1 is a heteroaryl group, it is other than a 5-methyl-isoxazolyl moiety.

38. A compound according to any one of claims 35 to 37, wherein A_1 is an aryl or heteroaryl moiety.

39. A compound according to any one of claims 35 to 38, wherein X is -CO- or -CO-NR', wherein R' is as defined in any one of claims 1 to 18, provided that when X is -CO-NR', the moiety -A₁-Y-A₂ is -phenyl-O-phenyl.

5

40. A compound according to any one of claims 35 to 39, wherein A₂ is other than a 4- to 10- membered saturated cycloalkyl ring, in which one of the carbon atoms is replaced by a N atom.

10 41. A compound according to any one of claims 35 to 40, wherein A₂ is a piperazinyl, pyridyl, pyrrolidinyl, pyrazinyl, cyclopropyl, phenyl or S,S-dioxo-thiomorpholino group which is unsubstituted or is substituted by a C₁-C₂ alkyl group.

15 42. A compound according to claim 35, wherein the benzodiazepine derivative of the formula (Ib) is:

6-(4-Methyl-piperazin-1-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-nicotinamide;

3,4,5,6-Tetrahydro-2H-[1,2']bipyridinyl-5'-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

20 (S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl-benzamide;

(S)-2-Chloro-4-morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-4-fluoro-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl-benzamide;

(S)-5-Chloro-2-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-5-fluoro-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

30 (S)-5-(4-Methyl-piperazin-1-ylmethyl)-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-5-Pyrrolidin-1-ylmethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-

1H-benzo[e][1,4]diazepin-3-yl)-amide;
(S)-5-Piperidin-1-ylmethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;
(S)-5-Dimethylaminomethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-
5 1H-benzo[e][1,4]diazepin-3-yl)-amide;
(S)-4-Fluoro-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-piperidin-1-yl-benzamide;
(S)-4-Fluoro-2-morpholino-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;
10 (S)-4-Cyano-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-pyrrolidin-1-yl-benzamide;
(S)-4-Cyano-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-piperidine-1-yl-benzamide;
(S)-N-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-pyrrolidin-1-
15 yl-4-trifluoromethyl-benzamide;
(S)-N-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-piperidin-1-yl-4-trifluoromethyl-benzamide;
(S)-2-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-4-trifluoromethyl-benzamide;
20 (S)-N-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-2-pyrrolidin-1-yl-5-trifluoromethyl-benzamide;
(S)-2-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-5-trifluoromethyl-benzamide;
(S)-2-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-
25 yl)-nicotinamide;
(S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-nicotinamide;
(S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-3-methyl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;
30 (S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-4-methyl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;
(S)-2-(1,1-Dioxo-1λ6-thiomorpholin-4-yl)-6-methyl-N-(2-oxo-5-phenyl-2,3-

dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-2-Chloro-6-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-3-Cyclopropyl-2-oxo-2,3-dihydro-imidazo[4,5-b]pyridine-1-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-3-(4-Methyl-piperazine-1-sulfonyl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-4-(4-Methyl-piperazin-1-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-N-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(piperidine-1-sulfonyl)-benzamide;

(S)-3-(Morpholine-4-sulfonyl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-5-Morpholin-4-ylmethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-5-Hydroxymethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-5-(1,1-Dioxo-1λ6-thiomorpholin-4-ylmethyl)-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-2-Chloro-4-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-2-Chloro-5-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-5-{[(2-Methanesulfonyl-ethyl)-methyl-amino]-methyl}-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-2-Pyridin-3-yl-thiazole-4-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-2-Pyridin-4-yl-thiazole-4-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-4-Methyl-2-pyrazin-2-yl-thiazole-5-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-2-Morpholin-4-ylmethyl-furan-3-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-

1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-3-Morpholin-4-ylmethyl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-5-Morpholin-4-ylmethyl-isoxazole-3-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-3-Morpholin-4-ylmethyl-furan-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-5-Pyridin-2-yl-thiophene-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-2-Methyl-4-(morpholin-4-sulfonyl)-furan-3-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-6-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-nicotinamide;

(S)-3-Morpholin-4-ylmethyl-thiophene-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

(S)-5-Morpholin-4-ylmethyl-thiophene-2-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide;

2-Morpholin-4-yl-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-benzamide;

(S)-5-Phenyl-oxazole-4-carboxylic acid (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-amide; or

1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(4-phenoxy-phenyl)-urea.

43. A compound according to any one of claims 35 to 42 for use in a method of treating the human or animal body.

44. A pharmaceutical composition comprising a compound according to any one of claims 35 to 43, and a pharmaceutically acceptable diluent or carrier.

45. A composition according to claim 44 comprising an optically active isomer of a compound according to any one of claims 35 to 42.

46. A composition according to claim 44 or 45 which is in the form of a tablet, troche, lozenge, aqueous or oily suspension, dispersible powders or granules.